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- (51) International Patent Classification<sup>7</sup>: A61K 9/50, 9/20 (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
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09/432,881 2 November 1999 (02.11.1999) US
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- (74) Agents: HEINES, M., Henry et al.; Townsend and Townsend and Crew LLP, 8th Floor, Two Embarcadero Center, San Francisco, CA 94111 (US).
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:  
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18 July 2002
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/032217 A3

(54) Title: PHARMACOLOGICAL INDUCEMENT OF THE FED MODE FOR ENHANCED DRUG ADMINISTRATION TO THE STOMACH

(57) Abstract: Drugs intended for absorption in the stomach or upper intestinal tract are administered in oral drug delivery systems in conjunction with any of various substances that have been discovered to function as potent agents for inducing the fed mode. By inducing the onset of the fed mode, these agents cause the stomach to prolong its retention of the drug delivery system, which is either large enough to be retained in the stomach during the fed mode or swells or expands to such a size upon ingestion. The fed mode inducing agents include the following compounds and their salts: glycine and glycylglycine, xylitol and related sugar alcohols, sodium and other metal docusates,  $\beta$ -casomorphins,  $\alpha$ -lipoic acid and similarly structured acids, 2,2-diaryl-4-(4'-aryl-4'-hydroxypiperidino)butyramides, arginine, Trp-Trp, alkylpyridinium halides, dihydroxybenzoic acids, and potent sweeteners such as aspartame, aspartic acid, acesulfame, and stevioside.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/30082

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61K9/50 A61K9/20

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, EMBASE, MEDLINE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 5 427 798 A (LUDWIG JENNIE SUE G ET AL) 27 June 1995 (1995-06-27)</p> <p>column 1, line 67 -column 2, line 12 column 2, line 40 -column 3, line 14 column 6, line 55 -column 7, line 16; example 1 claims 1-8</p> <p style="text-align: center;">--- -/--</p>	<p>1,2,5-9, 48-50, 97-99</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
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- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

15 April 2002

Date of mailing of the international search report

25. 04. 2002

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/30082

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP 1 029 892 A (SUWELACK SKIN & HEALTH CARE AG) 23 August 2000 (2000-08-23) page 2, column 1, line 3 - line 10 page 3, column 4, line 19 -page 4, column 5, line 16 page 7, column 12, line 58 -column 13, line 21 page 8, column 14, line 34 -page 9, column 16, line 48 page 10, column 18, line 13 -column 19, line 4 claims 1-3,29,31,35-38,40-42 ---	1,2,5-9, 48,97-99
X	EFENTAKIS M; AL-HMOUND H: "The influence of surfactants on drug release from a hydrophobic matrix" INTERNATIONAL JOURNAL OF PHARMACEUTICS, vol. 70, no. 1-2, 1991, pages 153-158, XP001064514 page 154, column 1, line 35 -column 2, line 28 page 155, column 2; figure 2 ---	1,2, 38-42
X	EP 0 715 846 A (RHONE-POULENC RORER GMBH) 12 June 1996 (1996-06-12)  page 7; example 5 ---	1,2, 5-13,47, 48,97-99
X	US 5 213 794 A (FRITSCH CHRISTIAN ET AL) 25 May 1993 (1993-05-25)  column 3, line 55 - line 61 column 6 -column 7; example 2 ---	1,2,5,6, 10-13, 47,48, 97-99
X	US 4 871 546 A (FELTZ DENNIS R ET AL) 3 October 1989 (1989-10-03)  column 1, line 14 - line 42 column 2 -column 3; example 1 ---	1,3-6, 14-16, 47,48, 52-54, 97-99
X	GB 1 330 829 A (SMITH KLINE FRENCH LAB) 19 September 1973 (1973-09-19)  page 2, column 1, line 22 - line 47 page 3, column 1, line 52 -page 4, column 1, line 12 --- -/--	1-8, 14-18, 47,97-99

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/30082

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>US 5 043 328 A (WEITHMANN KLAUS U) 27 August 1991 (1991-08-27)</p> <p>column 13 -column 14; examples 24,36 column 1, line 34 - line 38 column 16 -column 17; example 74 claim 1</p> <p style="text-align: center;">---</p>	<p>1,2,5,6, 23,24, 35-37</p>
X	<p>EP 0 571 217 A (MCNEIL PPC INC) 24 November 1993 (1993-11-24)</p> <p>page 9 -page 12; examples I,II figures 1-4 claims 1-10</p> <p style="text-align: center;">---</p>	<p>1-6, 27-31, 47-55, 97-99</p>
X	<p>US 4 470 980 A (HIGUCHI TAKERU ET AL) 11 September 1984 (1984-09-11)</p> <p>column 5 -column 7; examples 1,4,13,22,30,42 column 9; example 54 column 10, line 15 - line 21 claim 11</p> <p style="text-align: center;">---</p>	<p>1,2,5,6, 48,49, 97-99</p>
X	<p>STEPHENS J. AND CO: "Osmolyte and Tryptophan receptors controlling gastric emptying in the dog" AMERICAN JOURNAL OF PHYSIOLOGY, vol. 231, 1976, pages 848-853, XP001064412 cited in the application page 849, column 2, line 47 -page 850, column 1, line 4 page 850, column 2; figure 3 page 852, column 1, line 21 - line 30</p> <p style="text-align: center;">---</p>	<p>56-59</p>
A	<p>US 5 328 697 A (RAMAN SIVA N ET AL) 12 July 1994 (1994-07-12)</p> <p>column 1, line 40 - line 63 column 3, line 19 -column 5, line 14 column 5 -column 6; example 3 column 7 -column 8; examples 7,8 claims 1-3</p> <p style="text-align: center;">---</p>	<p>1-9, 32-34, 47-59, 82-84, 97-99</p>
A	<p>WO 99 25321 A (SMITHKLINE BEECHAM CORP ;VENKATESH GOPADI M (US)) 27 May 1999 (1999-05-27)</p> <p>page 10, line 30 -page 12, line 26; examples 5-7 claims 8,11,12</p> <p style="text-align: center;">---</p>	<p>1,2,5,6, 32-34, 48,49, 97-99</p>

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/30082

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 97 47285 A (DEPOMED INC ;SHELL JOHN W (US)) 18 December 1997 (1997-12-18) the whole document</p> <p>-----</p>	1-99

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/30082

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 56-96 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

As a result of the prior review under R. 40.2(e) PCT,  
no additional fees are to be refunded.

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☒ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 7-9,32-34,57-59,82-84

- 1.1. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 7-9,57-59

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and glycine, glycylglycine and salts thereof.

- 1.2. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 32-34,82-84

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and arginine and arginine salts.

- 1.3. Claims: partially claims 1-6,47-56,97-99  
A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and aspartic acid and salts thereof.

2. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 10-13,60-63

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and C4-C8 sugars alcohols.

3. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 14-18,64-68

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellaable polymer, and alkali and alkaline earth metal docusates.

4. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 19-22,69-72



## FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and beta-casomorphins.

5. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 23-26,73-76

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and dithioorganic acids of formula X as defined in the present application.

6. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 27-31,77-81

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and  
2,2-diaryl-4-(4'-aryl-4'-hydroxypiperidino)butyramides of formula X as defined in the present application.

7. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 35-37,85-87

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and the dipeptide Trp-Trp and salts thereof.

8. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 38-42,88-92

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and alkyl pyridinium halides of formula X as defined in the present application.

9. Claims: partially claims 1-6,47-56,97-99,  
entirely claims 43-46,93-96

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swellable polymer, and dihydroxybenzoic acids.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

**10. Claims: partially claims 1-6,47-56,97-99**

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swelling polymer, and stevioside.

**11. Claims: partially claims 1-6,47-56,97-99**

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swelling polymer, and alkyl esters of N-L-alpha-aspartyl L-phenylalanine.

**12. Claims: partially claims 1-6,47-56,97-99**

A single dosage form for oral administration that includes a solid-state drug in a solid matrix of a water-swelling polymer, and 3,4-dihydro-1,2,3-oxathiazin-4-ones of formula X as defined in the present application.

Please note that all inventions mentioned under item 1, although not necessarily linked by a common inventive concept, could be searched without effort justifying an additional fee.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/30082

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Information on patent family members

International Application No

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Information on patent family members

International Application No

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